POLICY BRIEF: The DolPHIN-2 Study (NCT03249181)

Background

- **1.5M HIV+ women** become pregnant every year
- A significant proportion of HIV-infected women in Africa **initiate ART late,** in the third trimester of pregnancy.
- Late ART initiation associated with a **seven-fold increased risk** of infant transmissions, and **doubling of infant mortality** in the first year of life

The DolPHIN-2 Study

- HIV+ pregnant women initiating ART in the **third trimester** randomised to **dolutegravir (DTG) vs efavirenz (EFV)** based therapy
- **Primary endpoint** was **VL<50 copies/mL at delivery** for efficacy, and occurrence of **drug toxicity in mothers and infants**.
- Efficacy and safety (to 31.1.19) data presented at Conference on Retroviruses and Opportunistic Infections (CROI) in Seattle on the 3rd March 2019.

Results

268 mothers (137 DTG, 131 EFV) included for safety, and 237 mothers (122 DTG, 115 EFV) for efficacy analyses

- **DTG associated with superior virological response when initiating ART in the third trimester**: VL<50 copies/mL in 74% (90/122) DTG versus 43% (49/115) EFV arm at delivery visit
- Risk ratio was unaffected by baseline VL, CD4 count, gestation at enrolment, maternal age, study site, and was 1.66 (95% CI 1.32 – 2.09) after a median of 55 days on ART.
- **DTG was well-tolerated in late pregnancy;** no differences in frequency or organ class of severe adverse events compared with EFV. No significant differences in gestational age, pre-term delivery, IRIS
- **No difference in congenital anomalies** between arms.

Poor outcomes related to late presentation included:

- **Four stillbirths** none thought to be related to drug
- **Eight infant deaths** none thought to be related to drug.
- **Three HIV infected infants** all likely to have occurred before ART initiation

Conclusion

- **DTG is well-tolerated and achieves superior virological suppression** before delivery compared to EFV when initiated in late pregnancy.
- Late presentation in pregnancy is associated with **poor outcomes** despite ART and regardless of arm.

What might this mean for policy makers ?

- For National Programmes where DTG is used as first-line (including pregnant women after the first trimester), no immediate change in policy is indicated, the availability of additional safety data is reassuring.
- National Programmes which discourage use of DTG in all pregnant women may wish to re-evaluate risk-benefit considerations. For women who present late in pregnancy, when fetal development has largely been completed, there are clear benefits in the rapid VL reduction achieved with DTG.
- National Programmes which do not routinely offer DTG to women of child-bearing potential may wish to re-evaluate the potential benefits of DTG outside the first trimester of pregnancy.
- Regardless of country policy, National Programmes should endeavour to **collect birth outcome data** on all pregnancy exposures to anti-retroviral drugs (including stillbirths and transmissions), contributing whenever possible to **international collaborative registries**.

For further information, see:

http://www.croiwebcasts.org/

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The DolPHIN-2 Study Group

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Notes:

1 DolPHIN-2 was funded by UNITAID
2 DTG was donated by ViiV Healthcare
3 The DolPHIN-2 Consortium includes the Infectious Diseases Institute (Kampala), The University of Cape Town, Radbourd University, Liverpool School of Tropical Medicine, and University of Liverpool